Report on principal results on aims of work under NASA Grant NsG-517 in the Department of Pathology, University of Minnesota, during the span from January 1, 1965, to June 30, 1965

- 1. In the mouse it was demonstrated that a number of circadian rhythms persist in animals completely deprived of food and water until the day of death from starvation and dehydration. Pertinent data on circadian rhythmic pituitary adrenocorticotropic activity, rectal temperature and pinnal mitosis of starving, dehydrated C mice were published in Reference 1 of the appended bibliography. Additional data demonstrating the same phenomenon have been obtained and summarized for the rhythm in liver glycogen and in serum and adrenal corticosterone of inbred C mice. Such information will be pertinent to designing the size of containers with the food supply for an extraterrestrial flight; e.g., in the rat experiment as it is now planned, provision is made for a two-day food supply so that this would be the maximal period for which a group of animals might be starving if a given cannister becomes non-functional. The work noted above demonstrates that the rhythms are demonstrable during such a period. This point will be of equal importance to any experiment on rodents, including the mouse experiment planned in work supported by the above grant.
- 2. Tests for transient predicted large phase-differences have been done for the study of a predicted desynchronization of several circadian rhythms in the mouse. Reference 2 of the appended bibliography notes this point for rhythms in rectal temperature, serum corticosterone and liver glycogen of inbred C mice on the basis of work done at the University of Minnesota, and for gross motor activity rhythm on data from inbred C mice sent from the University of Minnesota to the NASA Ames Research Center at Moffett Field, California, the data being obtained and examined first at Ames and analyzed thereafter at Minnesota.

This work provided evidence for the maintenance of the internal timing between several circadian rhythms in the free-running state. It served further for quantifying the predicted differences-in-phase at the predicted times-in the inbred C mouse. The above information will be important for spotchecks of rats recovered from extraterrestrial space and eventually from mice thus recovered, namely for spotchecks of certain neuroendocrine functions.

- 3. The maintenance of internal timing was documented for data on pulse and time estimation of a human being living for two months in the isolation of a cave, in the appended Reference No. 3. Further more extensive data, including indices of adrenal function, have been obtained for similar analyses on two additional subjects, each living in a separate cave, for periods of three and four months, respectively.
- 4. A number of computer techniques have been developed for the analysis of rhythms in biologic data--with displays of phase as a function of time--as indicated in the appended Reference 4.
- 5. Several rhythms with a frequency lower than circadian, some of them constituting apparently intrinsic aspects of human time structure, have been detected in certain steroidal metabolites of a healthy man (17-ketosteroid excretion) as indicated in appended References 5 and 6.
- 6. Some studies of the role played by neural functions in the maintenance of circadian endocrine rhythms have been summarized in appended Reference 7.

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